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U.S. Patent Operations/KLN
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EXAMINER	
HUYNH, PHUONG N	
ART UNIT	PAPER NUMBER
1644	6

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/931,704	Applicant(s) SENALDI, GIORGIO	
	Examiner " Neon" Phuong Huynh	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *31, and 36-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30 and 32-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-37 are pending.

2. Applicant's election with traverse of Group I, (Claims 1-30 and 32-35), drawn to a method of treating IgE-related disease comprising administering to a patient a therapeutically effective amount of an NNT-1 inhibitor, filed 2/25/02, is acknowledged. The traversal is on the grounds that (1) the method of Group I drawn to a method of treating using the NNT-1 inhibitor selected from a certain defined class of agents, (2) the method of Group II drawn to a method of diagnosing an IgE related disease using the NNT-1 inhibitor selected from a certain defined class of agents and (3) the searches for Group I and Group II would substantially overlap and impose no burden. This is not found persuasive because of the reasons set forth in the restriction mailed 11/26/01. Inventions of Groups I-II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the methods of treating (Group I) with distinct class of agents such as antagonist antibody, polypeptide, fusion polypeptide, soluble receptor proteins, anti-sense versus the method of diagnosing (Group II) using distinct products as recognized by applicant as a "defined class of agents" differ the with their respect to their process steps and endpoints. Therefore, they are patentably distinct. Further, the method of treating versus the method of diagnosing differs with respect to their Class and subclass. A search of Group I will not encompass Group II. It is a burden to search more than one invention. Therefore, the requirement of Group I (Claims 1-30 and 32-35) and Groups II-III is still deemed proper and is therefore made FINAL.

3. Claims 31 and 36-37 are withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

4. Claims 1-30 and 32-35 are being acted upon in this Office Action.

5. The drawings, filed 8/16/01, are not approved. Please see enclosed PTO 948, Notice of Draftsperson's Patent Drawing Review. Appropriate action is required.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-30 and 32-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification discloses only NNT-1 treatment increases antigen specific IgE in mice induced with anti-KLH and in NNT-1 transgenic mice (See pages 37-38 of the specification) and detection of anti-KLH IgE in *in vitro* (page 39). The specification discloses only a human NNT-1 polypeptide comprising the amino acid sequence of SEQ ID NO: 2 and a mouse NNT-1 polypeptide comprising the amino acid sequence of SEQ ID NO: 5 which encode by the polynucleotides of SEQ ID NO: 1 and 3, respectively. The specification on pages 17-18 defines the term NNT-1 inhibitor is any agent which is capable of inhibiting the production, activity, or expression of NNT-1 polypeptide and/or its receptor, including but not limited to ribozymes, and small molecules. The term "selective binding agents" refers to any molecule which a capable of specifically binding to an NNT-1 polypeptide, fragment, derivative or variant thereof or the NNT-1 receptor such as antibodies, derivative thereof, polypeptides, fusion polypeptides, part peptide, part antibody, soluble receptor proteins, small molecules, anti-sense oligonucleotides and other molecules having binding specificity. The specification defines the term "biological active fragment" on page 11 is any fragment from 1-20 amino acids from either the C-terminus or the N-terminus or both termini of the NNT-1 polypeptide that has qualitatively a substantially similar type of biological activity such as the ability to act as a growth factor for neurons and increases T and B cell production as the full length mature NNT-1 polypeptide where the activity is at least 50% of the activity of the full length polypeptide. The specification on page 12 defines the term "variant" as any NNT-1 polypeptide having one or more amino acid substitutions, deletions, and additions, any NNT-1 variants may have from 1 to 100 or more than 100 amino acid substitutions, insertions, additions and/or deletion.

However, the specification does not teach how to make and use (1) *any* NNT-1 inhibitor such as NNT-1 polypeptide or its receptor, ribozymes, small molecule, anti-sense oligonucleotides and other molecules having binding specificity toward NNT-1 polypeptide for a

method of treating any IgE-related disease such as allergic rhinitis, eczema, dermatitis, pollinosis, dermatitis, anaphylactic shock, and asthma, comprising administering to a patient a therapeutically effective amount of *any* NNT-1 inhibitor, *any* NNT-1 inhibitor is capable of inhibiting to at least one polypeptide comprising the amino acid sequences of SEQ ID NO: 2 or 5, *any* NNT-1 inhibitor is capable of inhibiting binding to at least one polypeptide encoded by a nucleic acid sequences of SEQ ID NO: 1 or 3, *any* NNT-1 inhibitor is capable of binding to a biologically active fragment of at least one polypeptide comprising the amino acid sequences of SEQ ID NO: 2 or 5 or at least one polypeptide encoded by a nucleic acid sequences of SEQ ID NO: 1 or 3, *any* NNT-1 inhibitor is capable of inhibiting the binding of *any* naturally occurring variant of polypeptides mentioned above, *any* NT-1 inhibitor is an NNT-1 expression modulator, *any* NNT-1 inhibitor is *any* selective binding agent, *any* NNT-1 inhibitor is *any* selective binding agent wherein the selective binding agent is *any* antibody or fragment thereof, *any* humanized antibody or fragment thereof, *any* antibody or fragment thereof having *any* human amino acid sequence, *any* antibody or fragment thereof having *any* human amino acid sequence and chemical modifications, *any* monoclonal antibody or fragment thereof, *any* polyclonal antibody or fragment thereof, *any* chimeric antibody or fragment thereof, *any* CDR-grafted antibody or fragment, *any* bispecific, single chain or heteroantibody or fragment thereof, *any* selective binding agent mentioned above further comprises *any* variable region fragment, *any* Fab, Fab', or F(ab) fragment, *any* selective binding agent mentioned above further comprises *any* Fc fragment, *any* selective binding agent mentioned above is bound to a detectable label, *any* selective binding agent mentioned above is produced from *any* hybridoma for a method of treating *any* IgE disease, (2) a method of modulating IgE levels in a patient comprising administering to said patient a therapeutically effective amount of *any* NNT-1 selective binding agent, (3) the said method wherein the selective binding agent is *any* antagonist antibody, (4) the said method wherein the selective binding agent reduces or inhibits the expression, activity or production of *any* NNT-1, (5) the said method wherein *any* NNT-1 selective binding agent reduces or inhibits the *in vivo* level of *any* NNT-1, (6) the said method wherein the level of IgE is inhibited, decreased or ameliorated, (7) a method of treating *any* allergic disease comprising administering to a patient a therapeutically effective amount of *any* NNT-1 inhibitor mentioned above, (8) the said method wherein the allergic disease is *any* type I allergic disease such as allergic rhinitis, eczema, dermatitis, pollinosis, and asthma, (9) a method of using *any* NNT-1 inhibitor mentioned above to modulate the levels of IgE in a patient, (10) a method of "preventing" *any* IgE-related disease

comprising administering to a patient a therapeutically effective amount of *any* NNT-1 inhibitor mentioned above and (11) the said method wherein the NTT-1 inhibitor is *any* antagonist antibody, *any* soluble receptor protein or *any* expression modulator.

There is no structure associated with the phrase "NNT-1 inhibitor". Given the infinite number of undisclosed "NNT-1 inhibitor" as encompassed by the claims, there is insufficient guidance and working examples as to which undisclosed "NNT-1 inhibitor" would be useful for treating, preventing or modulating any disease such as allergic disease mentioned above. Further, there is insufficient guidance and working examples as to which amino acid residue within the NNT-1 polypeptide of SEQ IN NO: 2 or 5 and fragment thereof mentioned above can be added, deleted, substitute and chemically modified and whether the resulting polypeptide, or fragment thereof would maintain the structure and function as NNT-1 of SEQ ID NO: 2 and 5, in turn, for a method of treating any IgE related diseases mentioned above, or modulating IgE levels in a patient. Finally, there is no disclosure of the polypeptide of any NNT-1 receptor, any nucleic acid encoding said NTT-1 receptor. Given the lack of in vivo treatment of any IgE-related disease using any undisclosed NNT-1 inhibitor, it follows that the method of preventing any disease such as type I allergic, IgE-related disease mentioned above is not enabled.

Ngo *et al* teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (See Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). Further, there are no in vivo working examples to demonstrate any "NNT-1 inhibitor" mentioned above would even bind specifically to the NNT-1 polypeptides of SEQ ID NO: 2 or 5, let alone using it to treat any IgE related disease, to suppress, inhibit or modulate the levels of IgE in a patient. In the absence of in vivo working examples, it is unpredictable for the following reasons: (1) the polypeptide or fragment thereof may be inactivated before producing an effect, i.e. such as inherently short half-life of the polypeptide or peptide; (2) the polypeptide or peptide may not reach the target area; and (3) other functional properties, known or unknown, may make the polypeptide or peptide unsuitable for *in vivo* therapeutic use. Therefore, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

With regard to NNT-1 inhibitor is an antagonist antibody, the specification fails to provide guidance (the specific amino acid sequence, binding specificity, the epitope to which the

antibody binds) as how to make such antibody with antagonistic activity for a method of treating any disease such as type I allergic disease mentioned above.

Kuby *et al* teach that antibody epitopes (B cell epitopes) are not linear and are comprised of complex three-dimentional array of scattered residues which will fold into specific conformation that contribute to binding (See Kuby 1994, page 94, in particular). Immunization with a peptide fragment derived from a full-length polypeptide may result in **antibody specificity** that differs from the antibody specificity directed against the native full-length polypeptide. Without the specific amino acid residues, it is unpredictable to determine which antibody generated from a "naturally-occurring variant" such as NNT-1 that may have 1 to 100 or more than 100 amino acid substitutions insertions, additions or deletions and fragment thereof will have the same antibody specificity as an antibody generated from the full-length polypeptide consisting of the amino acid sequence of SEQ ID NO: 2 or 5. Further, there are on in vivo working examples to demonstrate any of the undisclosed antibody mentioned above would inhibit, modulate IgE levels, in turn, for a method of treating IgE-related disease mentioned above.

The '370 patent teaches that the inherent problem with chimeric antibody has been a loss of affinity for the antigen, which means more antibody will have to be injected into a patient at higher cost and greater risk of adverse effects such as serum sickness (See column 2 lines 12-27, in particular). In the absence of in vivo working examples, it is unpredictable for the following reasons: (1) the antibody may be inactivated before producing an effect, i.e. such as inherently short half-life of the antibody; (2) the antibody may not reach the target area; and (3) other functional properties, known or unknown, may make the antibody unsuitable for *in vivo* therapeutic use, i.e. such as serum sickness which prohibitive to the use of antibody for such treatment.

With regard to NNT-1 inhibitor is a "soluble receptor protein" or "small molecule", applicant has not identified or isolated the receptor to which the claimed NNT-1 polypeptide binds. Further, there is no guidance as the amino acid sequence of any of the NNT-1 polypeptide receptor in the specification as filed. There are no in vivo working examples of treating any disease such as IgE related disease mentioned above comprising administering to a patient a therapeutically effective amount of *any* soluble NNT-1 receptor or small molecule. Since the soluble NNT-1 receptor has not been identified and the effectiveness of its antagonistic activity has not been demonstrated, it follows that the method of treating IgE-related disease mentioned above, or inhibiting or modulating the levels of IgE is not enable.

Debets *et al* teach that soluble receptors provide a natural source of highly selective cytokine inhibitors. However, apart from antagonizing cytokine activity, soluble receptors can also **agonize** cytokine activity thereby acting as "**double-edged sword**" (See page 456, column 3, Receptors, in particular). In an animal model for acute bronchial eosinophila, which is an IgE-related disease, eosinophilia (as a consequent of IgE increase) could be inhibited effectively using soluble IL-5 receptor (sIL-5R). However, sIL-4R superinduces IgE responses, even up to 3μg/ml of sIL-4R does not block the IL-4 induced synthesis of IgE (See page 457, column 1, last paragraph, bridging column 2, first paragraph, in particular). Debets *et al* further teach that the "double-edged sword" paradigm also applies to antibody against cytokine. Small complexes between such antibodies and cytokines are unable to activate complement and do not precipitate in vivo but are active as inflammatory complex (See page 547, column 3, second full paragraph, in particular). As with small molecule such as non-peptide antagonist, the only effective antagonist today has been isothiazolone, which interferes with IL-5 binding to its receptor (See page 456, column 3, second full paragraph, in particular). Given the indefinite number of undisclosed NNT-1 inhibitor, the lack of guidance and working examples, predicting which undisclosed soluble NNT-1 receptor would be useful for treating and preventing IgE-related disease mentioned above is unpredictable.

With regard to NNT-1 inhibitor is *any* "ribozyme", or "anti-sense oligonucleotide" that inhibits the expression, activity or production of *any* NNT-1, the specification as filed fails to provide *any* guidance as how to make and use *any* ribozyme, anti-sense oligonucleotide or small molecule mentioned above for inhibiting the expression, activity or production of *any* NNT-1 as a method of treating any or preventing any IgE-related disease mentioned above. There is a lack of *in vivo* working examples of using *any* "NNT-1 inhibitor" mentioned above. A ribozyme, or anti-sense oligonucleotide in the absence of *in vivo* data is unpredictable for the following reasons: (1) the stability and the **expression levels** of NNT-1 in vitro and in vivo has not been demonstrated; (2) the potential for adverse host immune response to said ribozyme, anti-sense oligonucleotide or small molecule has not been addressed; (3) the mode of administration or delivery of said NNT-1 inhibitor such as "ribozyme", or "anti-sense oligonucleotide" to the specific cell type have not been addressed; (4) the binding specificity of said NNT-1 inhibitor to specific cell types and (5) the "prevention" of IgE-related disease has not been demonstrated using any NNT-1 inhibitor mentioned above.

Verma *et al* teach that the inherent difficulties of gene therapy is the inability to deliver genes efficiently to the right type of cell, obtaining sustained expression or the lack thereof of the therapeutic protein without triggering the host immune responses (See page 239, in particular). Given the lack of guidance as to the specific nucleotide sequence and working examples, predicting which undisclosed NTT-1 inhibitor such as ribozyme, anti-sense oligonucleotide or small molecule mentioned above would be useful for treating and preventing IgE-related disease mentioned above is unpredictable.

For these reasons, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

8. Claims 1-30 and 32-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably convey to the artisan that the inventor had possession at the time of the ...claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the Applicants had possession at the time of invention of the claimed method of treating and preventing *any* IgE-related disease comprising administering to a patient a therapeutically effective amount of *any* NNT-1 inhibitor.

The specification does not reasonably provide a **written description** of (1) *any* NNT-1 inhibitor such as NNT-1 polypeptide or its receptor, ribozymes, small molecule, anti-sense oligonucleotides and other molecules having binding specificity toward NNT-1 polypeptide for a method of treating any IgE-related disease such as allergic rhinitis, eczema, dermatitis, pollinosis, dermatitis, anaphylactic shock, and asthma, comprising administering to a patient a therapeutically effective amount of *any* NNT-1 inhibitor, *any* NNT-1 inhibitor is capable of inhibiting to at least one polypeptide comprising the amino acid sequences of SEQ ID NO: 2 or 5, *any* NNT-1 inhibitor is capable of inhibiting binding to at least one polypeptide encoded by a nucleic acid sequences of SEQ ID NO: 1 or 3, *any* NNT-1 inhibitor is capable of binding to a

biologically active fragment of at least one polypeptide comprising the amino acid sequences of SEQ ID NO: 2 or 5 or at least one polypeptide encoded by a nucleic acid sequences of SEQ ID NO: 1 or 3, *any* NNT-1 inhibitor is capable of inhibiting the binding of *any* naturally occurring variant of polypeptides mentioned above, *any* NT-1 inhibitor is an NNT-1 expression modulator, *any* NNT-1 inhibitor is *any* selective binding agent, *any* NNT-1 inhibitor is *any* selective binding agent wherein the selective binding agent is *any* antibody or fragment thereof, *any* humanized antibody or fragment thereof, *any* antibody or fragment thereof having *any* human amino acid sequence, *any* antibody or fragment thereof having *any* human amino acid sequence and chemical modifications, *any* monoclonal antibody or fragment thereof, *any* polyclonal antibody or fragment thereof, *any* chimeric antibody or fragment thereof, *any* CDR-grafted antibody or fragment, *any* bispecific, single chain or heteroantibody or fragment thereof, *any* selective binding agent mentioned above further comprises *any* variable region fragment, *any* Fab, Fab', or F(ab) fragment, *any* selective binding agent mentioned above further comprises *any* Fc fragment, *any* selective binding agent mentioned above is bound to a detectable label, *any* selective binding agent mentioned above is produced from *any* hybridoma for a method of treating *any* IgE disease, (2) a method of modulating IgE levels in a patient comprising administering to said patient a therapeutically effective amount of *any* NNT-1 selective binding agent, (3) the said method wherein the selective binding agent is *any* antagonist antibody, (4) the said method wherein the selective binding agent reduces or inhibits the expression, activity or production of *any* NNT-1, (5) the said method wherein *any* NNT-1 selective binding agent reduces or inhibits the *in vivo* level of *any* NNT-1, (6) the said method wherein the level of IgE is inhibited, decreased or ameliorated, (7) a method of treating *any* allergic disease comprising administering to a patient a therapeutically effective amount of *any* NNT-1 inhibitor mentioned above, (8) the said method wherein the allergic disease is *any* type I allergic disease such as allergic rhinitis, eczema, dermatitis, pollinosis, and asthma, (9) a method of using *any* NNT-1 inhibitor mentioned above to modulate the levels of IgE in a patient, (10) a method of "preventing" *any* IgE-related disease comprising administering to a patient a therapeutically effective amount of *any* NNT-1 inhibitor mentioned above and (11) the said method wherein the NTT-1 inhibitor is *any* antagonist antibody, *any* soluble receptor protein or *any* expression modulator.

The specification discloses only NNT-1 treatment increases antigen specific IgE in mice induced with anti-KLH and in NNT-1 transgenic mice (See pages 37-38 of the specification) and detection of anti-KLH IgE in *in vitro* (page 39). The specification discloses only a human NNT-1

polypeptide comprising the amino acid sequence of SEQ ID NO: 2 and a mouse NNT-1 polypeptide comprising the amino acid sequence of SEQ ID NO: 5 which encode by the polynucleotides of SEQ ID NO: 1 and 3, respectively. There is insufficient written description about the structure associated with function of any NTT-1 inhibitor for treating any disease such as Type I allergic disease mentioned above. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

10. Claims 2, 6-7 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "SEQ ID NO: 4" in claim 2 is indefinite and ambiguous. The specification discloses SEQ ID NO: 4 is a DNA and not an amino acid sequence.

The recitation of "having a human amino acid sequence" in claims 6-7 is ambiguous and indefinite. As written, it is not clear which specific human amino acid sequence applicant intends to claim. One of ordinary skill in the art cannot appraise the metes and bounds of the claimed invention.

The recitation of "human chemical modification" in claim 7 is indefinite and ambiguous. One of ordinary skill in the art cannot appraise the metes and bounds of the claimed invention.

11. Claims 1-30 and 32-35 are free of prior art.

12. No Claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

14. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
May 20, 2002

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